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Applicant: Podos et al.

TECH CENTER 1600/2900

Serial No.: 09/073,552

Examiner: Fay, Z.

Filed: May 6, 1998

Group Art Unit: 1644

For: 8-ISO-PROSTAGLANDINS FOR GLAUCOMA THERAPY

#11
JRP
11/2/99

RESPONSE TO FINAL ACTION

I hereby certify that this paper is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C., 20231.

October 20, 1999

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Signature

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October 20, 1999
Date of Signature

Assistant Commissioner of Patents
Washington, D.C. 20231

SIR:

In response to the Official Action dated July 20, 1999, please consider the following remarks. Applicants enclose herewith a Notice of Appeal of claims 1-21, together with the appropriate fee.

Claims 1-21 are pending. The Examiner has maintained the rejection of all claims as obvious under 35 U.S.C. §103 over Schneider, United States Patent No. 5,631,287. In particular, the Examiner states:

Applicant alleges criticality to the trans configuration of the prior art compounds in comparison to the cis compounds of the instant application. Applicant is reminded that cis and trans of a compound usually share the same type of activity with the [sic] different degrees of potency. The fact that they show their activity

with different mechanism [*sic*] does not create a patentably distinct use. Applicant has presented no evidence to the advantages of the claimed *cis* compounds over the *trans* used by the prior art in treating macular edema.¹ Therefore the prior rejection sustains.

Applicants assert that the claims are not obvious over Schneider. While the Examiner's statements might be correct applied to **optical isomers**, they do not apply to **geometric isomers**, such as the *cis* compounds of the present invention and the *trans* compounds disclosed in Schneider. A classic example of geometric isomerism involving *cis* or *trans* substituents on adjacent carbon atoms of a ring is provided by the hexopyranose sugars, glucose and galactose, which have the same structural atom sequence. In glucose, the substituents on ring carbon atoms 3 and 4 are *trans* with respect to each other and the plane of the ring. However, galactose differs from glucose only in that the C3 and C4 substituents are *cis* in their relationship (see Exhibit A, a copy of Table 25.1 from Streitwieser and Heathcock, 1976, *An Introduction to Organic Chemistry*, MacMillan Publishing Co., New York, p. 697, which shows the Fischer projections for both molecules). As a consequence of the geometric isomerism, glucose and galactose have completely different physical, chemical, and biological properties (see Exhibit B, p. 702 of Streitwieser and Heathcock; *supra*, which discusses enzyme specificities relating to carbohydrate structure).

Thus the relationship between glucose and galactose is analogous to that of the prostaglandins of the invention, in which the substituents on adjacent ring carbon atoms (C8 and C12) are *cis*, and the prostaglandins of Schneider, where the substituents are *trans* at the corresponding positions. Therefore, based on the glucose/galactose example and numerous other examples of geometric isomerism, there is no basis for the expectation that the biological properties of a pair of such isomers, such as PGE₂ and iso-PGE₂, differ only in degree. Indeed,

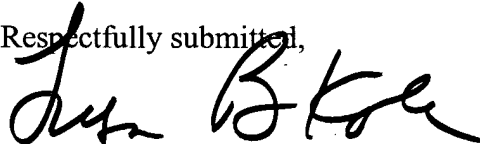
¹ Applicants presume that the Examiner intended to refer to "increased intraocular pressure".

data provided in the instant specification (see Table 1 on page 10 and page 9 at lines 12-17) demonstrates that the 8-iso prostaglandin derivatives have a different pharmacologic profile than do the prostaglandins with the opposite geometric structure. Namely, the prostaglandins of the invention act on trabecular meshwork cells and not via a uveoscleral mechanism (which is the site of action of prostaglandins, like latanoprost, that do not have the 8-iso geometry; see, *e.g.*, the instant specification at page 3 lines 9-13, page 4 lines 3-5), indicating that they act on different receptor systems than the isomeric prostaglandins with *trans* geometry of the C8 and C12 substituents.

For all the foregoing reasons, the claims are not obvious and the rejection should be withdrawn.

An early allowance is earnestly requested.

Respectfully submitted,



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